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Talc, NTP TR 421

TABLE C2

Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Talc: 6 mg/m³ (continued)

Number of Days on Study	2	2	3	4	5	5	5	5	5	5	5	6	6	6	6	6	7	7	7	7	7	7	7
	5	5	4	2	4	5	5	8	9	9	2	2	3	8	8	8	1	1	2	3	3	3	3
	3	3	4	3	6	0	8	4	0	1	4	6	3	1	5	8	0	9	2	6	6	6	6
Carcass ID Number	0	1	0	0	1	1	0	1	1	1	0	0	0	1	1	0	0	1	1	0	0	0	0
	3	3	4	0	2	6	4	5	5	2	4	7	3	5	0	6	1	5	3	0	0	0	0
	5	3	2	7	1	4	0	1	6	9	1	4	8	7	0	1	5	4	2	1	4	5	8
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
General Body System																							
Tissue NOS	+ + +																						
Genital System																							
Epididymis	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Preputial gland	+ +																						
Prostate	+	+	M	A	I	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Testes	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Hematopoietic System																							
Bone marrow	+	+	+	+	A	A	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Lymph node, bronchial	+	+	+	+	M	+	I	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+
Lymph node, mandibular	M	M	+	M	M	+	+	+	+	M	+	M	M	M	+	M	+	+	+	+	M	M	M
Lymph node, mediastinal	M	M	M	M	M	+	M	M	M	+	M	M	M	M	M	M	M	M	M	+	M	M	M
Lymph node, mesenteric	M	M	M	M	+	M	+	+	+	+	+	M	+	+	+	M	+	+	+	+	M	+	+
Spleen	A	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	A	M	M	M	+	+	+	I	+	+	M	+	M	+	I	M	+	+	+	+	+	+	+
Integumentary System																							
Mammary gland	M	M	M	M	M	A	M	M	M	M	M	M	M	M	M	+	M	+	+	M	+	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																							
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																							
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																							
Larynx	A	+	+	A	+	A	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	I	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																							
Alveolar/bronchiolar carcinoma	X																						
Hepatocellular carcinoma, metastatic, liver																							
Nose	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	A	I	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+

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TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Talc: 6 mg/m³ (continued)

Number of Days on Study	2	2	3	4	5	5	5	5	5	5	6	6	6	6	6	6	7	7	7	7	7	7	7
	5	5	4	2	4	5	5	8	9	9	2	2	3	8	8	8	1	1	2	3	3	3	3
	3	3	4	3	6	0	8	4	0	1	4	6	3	1	5	8	0	9	2	6	6	6	6
Carcass ID Number	0	1	0	0	1	1	0	1	1	1	0	0	0	1	1	0	0	1	1	0	0	0	0
	3	3	4	0	2	6	4	5	5	2	4	7	3	5	0	6	1	5	3	0	0	0	0
	5	3	2	7	1	4	0	1	6	9	1	4	8	7	0	1	5	4	2	1	4	5	8
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Special Senses System	None																						
Urinary System																							
Kidney	+ + + + + A + + + + + + + + + + + + + + + + +																						
Urinary bladder	A + + A + A A A + + + + A + A + A + + + + + +																						
Systemic Lesions																							
Multiple organs	+ +																						
Lymphoma malignant lymphocytic	X																						

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Talc, NTP TR 421

TABLE C3

Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Talc

	0 mg/m ³	6 mg/m ³	18 mg/m ³
Harderian Gland: Adenoma			
Overall rates ^a	1/46 (2%)	0/47 (0%)	4/49 (8%)
Adjusted rates ^b	3.3%	0.0%	12.0%
Terminal rates ^c	1/30 (3%)	0/28 (0%)	3/32 (9%)
First incidence (days)	736 (I)	- ^e	725
Life table tests	P=0.073	P=0.514N	P=0.204
Logistic regression tests ^d	P=0.075	P=0.514N	P=0.216
Cochran-Armitage test ^d	P=0.065		
Fisher exact test ^d		P=0.495N	P=0.201
Liver: Hepatocellular Adenoma			
Overall rates	3/45 (7%)	9/47 (19%)	4/48 (8%)
Adjusted rates	10.0%	29.5%	11.8%
Terminal rates	3/30 (10%)	7/28 (25%)	3/32 (9%)
First incidence (days)	736 (I)	633	672
Life table tests	P=0.489N	P=0.050	P=0.539
Logistic regression tests	P=0.493N	P=0.061	P=0.552
Cochran-Armitage test	P=0.515N		
Fisher exact test		P=0.070	P=0.536
Liver: Hepatocellular Carcinoma			
Overall rates	6/45 (13%)	5/47 (11%)	11/48 (23%)
Adjusted rates	16.7%	13.7%	27.3%
Terminal rates	2/30 (7%)	1/28 (4%)	5/32 (16%)
First incidence (days)	571	546	438
Life table tests	P=0.114	P=0.491N	P=0.187
Logistic regression tests	P=0.116	P=0.445N	P=0.203
Cochran-Armitage test	P=0.097		
Fisher exact test		P=0.469N	P=0.177
Liver: Hepatocellular Adenoma or Carcinoma			
Overall rates	9/45 (20%)	13/47 (28%)	14/48 (29%)
Adjusted rates	25.6%	38.1%	34.5%
Terminal rates	5/30 (17%)	8/28 (29%)	7/32 (22%)
First incidence (days)	571	546	438
Life table tests	P=0.256	P=0.228	P=0.230
Logistic regression tests	P=0.216	P=0.257	P=0.223
Cochran-Armitage test	P=0.225		
Fisher exact test		P=0.269	P=0.217
Lung: Alveolar/bronchiolar Adenoma			
Overall rates	6/45 (13%)	4/47 (9%)	9/48 (19%)
Adjusted rates	20.0%	14.3%	27.0%
Terminal rates	6/30 (20%)	4/28 (14%)	8/32 (25%)
First incidence (days)	736 (I)	736 (I)	672
Life table tests	P=0.224	P=0.411N	P=0.333
Logistic regression tests	P=0.251	P=0.411N	P=0.371
Cochran-Armitage test	P=0.210		
Fisher exact test		P=0.342N	P=0.336

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Lesions in Male Mice

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TABLE C3

Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Talc (continued)

	0 mg/m ³	6 mg/m ³	18 mg/m ³
Lung: Alveolar/bronchiolar Carcinoma			
Overall rates	7/45 (16%)	2/47 (4%)	2/48 (4%)
Adjusted rates	23.3%	5.9%	5.2%
Terminal rates	7/30 (23%)	1/28 (4%)	0/32 (0%)
First incidence (days)	736 (T)	558	438
Life table tests	P=0.068N	P=0.093N	P=0.068N
Logistic regression tests	P=0.069N	P=0.073N	P=0.070N
Cochran-Armitage test	P=0.065N		
Fisher exact test		P=0.069N	P=0.065N
Lung: Alveolar/bronchiolar Adenoma or Carcinoma			
Overall rates	12/45 (27%)	5/47 (11%)	11/48 (23%)
Adjusted rates	40.0%	16.4%	30.8%
Terminal rates	12/30 (40%)	4/28 (14%)	8/32 (25%)
First incidence (days)	736 (T)	558	438
Life table tests	P=0.533N	P=0.063N	P=0.426N
Logistic regression tests	P=0.552N	P=0.043N	P=0.423N
Cochran-Armitage test	P=0.554N		
Fisher exact test		P=0.043N	P=0.429N
Pituitary Gland (Pars Intermedia): Adenoma			
Overall rates	0/44 (0%)	2/44 (5%)	0/46 (0%)
Adjusted rates	0.0%	6.5%	0.0%
Terminal rates	0/29 (0%)	1/27 (4%)	0/32 (0%)
First incidence (days)	-	681	- ^f
Life table tests	P=0.547N	P=0.238	-
Logistic regression tests	P=0.566N	P=0.239	-
Cochran-Armitage test	P=0.564N		
Fisher exact test		P=0.247	-
Spleen: Hemangiosarcoma			
Overall rates	2/44 (5%)	0/44 (0%)	2/47 (4%)
Adjusted rates	6.9%	0.0%	5.5%
Terminal rates	2/29 (7%)	0/28 (0%)	0/32 (0%)
First incidence (days)	736 (T)	-	672
Life table tests	P=0.595	P=0.246N	P=0.650N
Logistic regression tests	P=0.581	P=0.246N	P=0.668N
Cochran-Armitage test	P=0.577		
Fisher exact test		P=0.247N	P=0.666N
All Organs: Hemangiosarcoma			
Overall rates	4/46 (9%)	0/47 (0%)	3/49 (6%)
Adjusted rates	12.9%	0.0%	8.4%
Terminal rates	3/30 (10%)	0/28 (0%)	1/32 (3%)
First incidence (days)	710	-	672
Life table tests	P=0.529N	P=0.071N	P=0.448N
Logistic regression tests	P=0.545N	P=0.060N	P=0.456N
Cochran-Armitage test	P=0.554N		
Fisher exact test		P=0.056N	P=0.464N

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TABLE C3

Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Talc (continued)

	0 mg/m ³	6 mg/m ³	18 mg/m ³
All Organs: Hemangioma or Hemangiosarcoma			
Overall rates	4/46 (9%)	0/47 (0%)	4/49 (8%)
Adjusted rates	12.9%	0.0%	11.4%
Terminal rates	3/30 (10%)	0/28 (0%)	2/32 (6%)
First incidence (days)	710	—	672
Life table tests	P=0.515	P=0.071N	P=0.590N
Logistic regression tests	P=0.505	P=0.060N	P=0.598N
Cochran-Armitage test	P=0.492		
Fisher exact test		P=0.056N	P=0.607N
All Organs: Malignant Lymphoma (Lymphocytic, Mixed, or Undifferentiated Cell Type)			
Overall rates	5/46 (11%)	1/47 (2%)	0/49 (0%)
Adjusted rates	16.7%	3.6%	0.0%
Terminal rates	5/30 (17%)	1/28 (4%)	0/32 (0%)
First incidence (days)	736 (I)	736 (I)	—
Life table tests	P=0.019N	P=0.116N	P=0.027N
Logistic regression tests	P=0.019N	P=0.116N	P=0.027N
Cochran-Armitage test	P=0.020N		
Fisher exact test		P=0.097N	P=0.024N
All Organs: Benign Tumors			
Overall rates	11/46 (24%)	16/47 (34%)	18/49 (37%)
Adjusted rates	35.2%	51.1%	51.4%
Terminal rates	10/30 (33%)	13/28 (46%)	15/32 (47%)
First incidence (days)	587	633	672
Life table tests	P=0.158	P=0.135	P=0.127
Logistic regression tests	P=0.154	P=0.188	P=0.138
Cochran-Armitage test	P=0.139		
Fisher exact test		P=0.199	P=0.128
All Organs: Malignant Tumors			
Overall rates	20/46 (43%)	8/47 (17%)	15/49 (31%)
Adjusted rates	58.3%	23.3%	35.9%
Terminal rates	16/30 (53%)	4/28 (14%)	6/32 (19%)
First incidence (days)	571	546	438
Life table tests	P=0.253N	P=0.012N	P=0.166N
Logistic regression tests	P=0.262N	P=0.005N	P=0.152N
Cochran-Armitage test	P=0.245N		
Fisher exact test		P=0.005N	P=0.139N
All Organs: Benign or Malignant Tumors			
Overall rates	26/46 (57%)	20/47 (43%)	28/49 (57%)
Adjusted rates	76.2%	58.0%	66.5%
Terminal rates	22/30 (73%)	14/28 (50%)	18/32 (56%)
First incidence (days)	571	546	438
Life table tests	P=0.442	P=0.208N	P=0.554
Logistic regression tests	P=0.344	P=0.102N	P=0.503
Cochran-Armitage test	P=0.399		
Fisher exact test		P=0.127N	P=0.558

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Lesions in Male Mice

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TABLE C3

Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Talc (continued)

(T) Terminal sacrifice

^a Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.

^b Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality

^c Observed incidence at terminal kill

^d Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.

^e Not applicable; no tumors in animal group

^f Value of statistic cannot be computed.

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Talc, NTP TR 421

TABLE C4

Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Talc^a

	0 mg/m ³	6 mg/m ³	18 mg/m ³
Disposition Summary			
Animals initially in study	50	50	50
Early deaths			
Moribund	1	2	3
Natural deaths	16	18	14
Survivors			
Terminal sacrifice	30	28	32
Missexed	1	1	0
Missing	2	1	1
Animals examined microscopically	46	47	49
Alimentary System			
Gallbladder	(31)	(29)	(35)
Dilatation			1 (3%)
Epithelium, hyperplasia, papillary			1 (3%)
Intestine large, cecum	(34)	(35)	(37)
Hyperplasia, lymphoid		1 (3%)	3 (8%)
Intestine large, colon	(36)	(38)	(39)
Hyperplasia, lymphoid	1 (3%)		
Intestine large, rectum	(32)	(32)	(31)
Serosa, inflammation, suppurative		1 (3%)	
Intestine small, duodenum	(32)	(30)	(34)
Hyperplasia, lymphoid			1 (3%)
Mucosa, atrophy	3 (9%)	7 (23%)	3 (9%)
Intestine small, ileum	(33)	(32)	(35)
Hyperplasia, lymphoid	5 (15%)	3 (9%)	5 (14%)
Mucosa, atrophy	3 (9%)	5 (16%)	4 (11%)
Peyer's patch, necrosis	1 (3%)		
Intestine small, jejunum	(32)	(31)	(36)
Hyperplasia, lymphoid			1 (3%)
Mucosa, atrophy	3 (9%)	3 (10%)	2 (6%)
Liver	(45)	(47)	(48)
Abscess	1 (2%)		1 (2%)
Focal cellular change	4 (9%)	3 (6%)	5 (10%)
Hematocyst		1 (2%)	
Hematopoietic cell proliferation	2 (4%)	2 (4%)	
Infarct	2 (4%)		
Inflammation, focal		3 (6%)	1 (2%)
Mineralization, focal		1 (2%)	
Necrosis, focal	4 (9%)	5 (11%)	4 (8%)
Pigmentation, hemosiderin, focal			1 (2%)
Bile duct, hyperplasia, focal			1 (2%)
Serosa, inflammation, suppurative			1 (2%)
Pancreas	(42)	(39)	(42)
Serosa, inflammation, suppurative			1 (2%)
Stomach, forestomach	(43)	(41)	(46)
Hyperplasia, squamous, focal		1 (2%)	1 (2%)
Tooth		(3)	
Dysplasia		3 (100%)	
Cardiovascular System			
Heart	(45)	(46)	(49)
Thrombosis		1 (2%)	1 (2%)
Coronary artery, mineralization		1 (2%)	
Myocardium, degeneration, focal	1 (2%)		
Myocardium, fibrosis, focal		1 (2%)	

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Lesions in Male Mice

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TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Talc (continued)

	0 mg/m ³	6 mg/m ³	18 mg/m ³
Endocrine System			
Adrenal gland	(43)	(46)	(47)
Spindle cell, hyperplasia	38 (88%)	37 (80%)	35 (74%)
Adrenal gland, cortex	(43)	(46)	(47)
Atrophy	1 (2%)		
Hyperplasia, focal		1 (2%)	
Vacuolization cytoplasmic, focal		3 (7%)	4 (9%)
Parathyroid gland	(25)	(21)	(26)
Cyst	3 (12%)	1 (5%)	
Pituitary gland	(44)	(44)	(46)
Cyst	1 (2%)		1 (2%)
Pigmentation, lipofuscin	1 (2%)		
Thyroid gland	(45)	(46)	(45)
Cyst	2 (4%)	1 (2%)	1 (2%)
Follicular cell, hyperplasia	4 (9%)	8 (17%)	8 (18%)
General Body System			
None			
Genital System			
Epididymis	(39)	(39)	(42)
Inflammation, suppurative	1 (3%)	1 (3%)	
Preputial gland	(8)	(6)	(8)
Dilatation	7 (88%)	6 (100%)	8 (100%)
Inflammation	3 (38%)		1 (13%)
Prostate	(40)	(43)	(44)
Inflammation, suppurative	3 (8%)	7 (16%)	4 (9%)
Epithelium, hyperplasia		1 (2%)	
Seminal vesicle	(41)	(43)	(39)
Inflammation, suppurative		2 (5%)	1 (3%)
Testes	(43)	(44)	(45)
Aspermatogenesis, diffuse			1 (2%)
Atrophy, diffuse			1 (2%)
Hypospermia	1 (2%)	2 (5%)	
Inflammation, suppurative		1 (2%)	
Seminiferous tubule, degeneration, focal	3 (7%)	4 (9%)	1 (2%)
Hematopoietic System			
Bone marrow	(40)	(42)	(43)
Hyperplasia	4 (10%)	1 (2%)	1 (2%)
Myelofibrosis	2 (5%)	2 (5%)	
Myeloid cell, hyperplasia	4 (10%)	7 (17%)	1 (2%)
Lymph node	(45)	(46)	(48)
Iliac, hyperplasia, lymphoid	1 (2%)		
Iliac, hyperplasia, plasma cell	1 (2%)		
Lumbar, hyperplasia, lymphoid	1 (2%)	1 (2%)	
Lumbar, hyperplasia, plasma cell		1 (2%)	
Pancreatic, inflammation, granulomatous		1 (2%)	
Renal, depletion lymphoid			1 (2%)
Renal, hyperplasia, lymphoid			1 (2%)

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Talc, NTP TR 421

TABLE C4

Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Talc (continued)

	0 mg/m ³	6 mg/m ³	18 mg/m ³
Hematopoietic System (continued)			
Lymph node, bronchial	(32)	(39)	(44)
Abscess			1 (2%)
Hyperplasia, histiocytic	1 (3%)	32 (82%)	42 (95%)
Hyperplasia, histiocytic, lymphoid		1 (3%)	
Hyperplasia, lymphoid	3 (9%)	10 (26%)	23 (52%)
Infiltration cellular, mixed cell	3 (9%)	1 (3%)	3 (7%)
Inflammation, acute	1 (3%)		
Follicular, necrosis	1 (3%)		
Lymph node, mandibular	(23)	(23)	(19)
Hyperplasia, histiocytic		1 (4%)	
Hyperplasia, lymphoid			1 (5%)
Follicular, necrosis			1 (5%)
Lymph node, mediastinal	(9)	(10)	(7)
Hyperplasia, histiocytic	1 (11%)	1 (10%)	2 (29%)
Hyperplasia, lymphoid		2 (20%)	
Lymph node, mesenteric	(36)	(39)	(40)
Depletion lymphoid	1 (3%)		2 (5%)
Hyperplasia, lymphoid	4 (11%)	3 (8%)	6 (15%)
Infiltration cellular, mixed cell	18 (50%)	20 (51%)	13 (33%)
Inflammation, granulomatous		1 (3%)	
Thrombosis			1 (3%)
Follicular, necrosis		6 (15%)	2 (5%)
Spleen	(44)	(44)	(47)
Hematocyst		1 (2%)	
Hematopoietic cell proliferation	6 (14%)	7 (16%)	10 (21%)
Hyperplasia, lymphoid	3 (7%)	2 (5%)	3 (6%)
Hyperplasia, mast cell			1 (2%)
Inflammation, granulomatous		1 (2%)	
Lymphoid follicle, depletion lymphoid		2 (5%)	5 (11%)
Lymphoid follicle, necrosis	2 (5%)	5 (11%)	1 (2%)
Thymus	(34)	(33)	(40)
Cyst	3 (9%)	2 (6%)	1 (3%)
Hyperplasia, lymphoid			1 (3%)
Inflammation, granulomatous		1 (3%)	
Necrosis	1 (3%)		2 (5%)
Cortex, depletion lymphoid	6 (18%)	10 (30%)	8 (20%)
Epithelial cell, hyperplasia, focal	1 (3%)		
Integumentary System			
Skin	(44)	(45)	(48)
Abscess		1 (2%)	
Alopecia	1 (2%)		1 (2%)
Inflammation, acute		2 (4%)	
Ulcer, focal		2 (4%)	
Musculoskeletal System			
Bone	(46)	(47)	(49)
Rib, cartilage, fracture healed	1 (2%)		
Nervous System			
Brain	(46)	(47)	(48)
Mineralization, focal	37 (80%)	39 (83%)	38 (79%)

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